Use of the Artificial Kidney in Snakebite

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AT 1:40 P.M. on October 19, 1959, a 33-year-old Mexican laborer was bitten on the calf of the right leg by a rattlesnake that was later identified as Crotalus rubor rubor, or red diamond rattlesnake.[3] Fifteen minutes later at a nearby hospital the patient was noted to be frothing at the mouth, was tense and irritable and had generalized muscle fasciculation. Oral temperature was 101° F. A single fang mark was present on the right calf. Immediate treatment consisted of 1,500 units of tetanus antitoxin, 75 milligrams of hydrocortisone sodium succinate (Solu-Cortef®), cold compresses to the right calf and 1 vial of Crotalus antivenin, half locally around the bite and half intramuscularly. No incision of the wound was made. The hemoglobin was 15.1 grams per 100 cc. and leukocytes numbered 27,000 per cu. mm. The following morning the oral temperature was 104° F., the pulse rate 170 and blood pressure 120/80 millimeters of mercury. Extensor rigidity suggesting ospisthotonos was present. There were no conjunctival hemorrhages. The pupils were pinpoint and the optical fundi were not visualized. No abnormalities of lymph nodes, heart, lungs or abdomen were noted. The deep tendon reflexes were decreased. Plantar reflexes were within normal limits. There was no localized tenderness, redness or swelling about the site of the bite. In spite of heavy sedation, soft restraints were required for the safety of the patient.

Penicillin was administered and cooling measures carried out and by noon the temperature was 99° F. Hematemesis, hematuria and oliguria had developed, however. A total of 5 vials of antivenin, 1,500 units of tetanus antitoxin and 1,200,000 units of penicillin were given during the first 24 hours. At no time was hypotension observed. In the eight hours from 7 a.m. to 3 p.m. on October 20, 1959, the patient's fluid intake was 4,000 milliliters and urinary output 290 milliliters. He was transferred to the San Diego County General Hospital for further observation and treatment.

On admission palpable right inguinal lymph nodes were present and erythema extended from the site of the bite in a linear fashion up the right calf, but no significant necrosis or swelling at the area of inoculation was present. An electrocardiogram was within normal limits. The urine was brown and strongly positive for albumin and hemolyzed red blood cells. Bleeding and coagulation times were 1 and 3 minutes. Prothrombin time was 96 per cent of normal. The fibrinogen level was 0.5 gram per 100 cc. No significant change occurred in hemoglobin values during the the first 96 hours. Hyperkalemia did not become a problem.

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The patient remained oliguric; urine output for each of the succeeding four days was 500 ml., 225 ml., 125 ml. and 80 ml. When symptoms of uremic deterioration developed on the morning of the sixth day, dialysis was carried out for five hours with a disposable twin-coil artificial kidney. Transient systolic hypertension—160 millimeters of mercury—developed at the end of the procedure. The blood urea nitrogen was reduced from 138 mg. to 54 mg. per 100 cc. Oliguria continued and on the tenth hospital day dialysis for five hours was again carried out. As before, transient systolic hypertension developed, this time to 180 mm. of mercury. The blood urea nitrogen, 134 mg. per 100 cc. before dialysis, was 54 mg. after the procedure.

Progressive diuresis occurred and by the 17th hospital day the urine output was 6,000 milliliters per 24 hours. In spite of this, the blood urea nitrogen rose to 166 mg. per 100 cc. Then, with diuresis continuing, the chemical contents of the blood returned to normal limits in the next ten days.

On the 18th hospital day the blood pressure rose to 220/100 mm. of mercury. He had right-sided Jacksonian seizures and pneumothorax developed on the left side. The hypertension responded to intravenous magnesium sulfate and sodium amytal. Aspiration and suction drainage reduced the pneumothorax and recovery was uneventful. The patient was discharged on the 35th hospital day, feeling well. The blood pressure and results of urinalysis were within normal limits.

DISCUSSION

There are an estimated 1,500 cases of venomous snake bite in the United States each year, approximately 70 per cent of them by rattlesnakes. Death occurs in from 1.5 to 3 per cent of cases. Early death from intravenous inoculation of Crotalus venom is usually due to hemolytic shock or hemorrhage, or to central nervous system intoxication. Later, renal failure may become a significant factor.

What are the components of Crotalus venom responsible for the production of renal failure? The important hemolytic principle in Crotalus venom is the enzyme *lecithinase*. This substance converts the lecithin of the red blood cells or plasma to the hemolytic agent *lysolecithin*, which acts by injuring the red blood cell membrane, causing hemolysis. This or a similar substance may also act directly on the vascular endothelium to permit diapedesis of red blood cells into tissue spaces.

Proteases convert prothrombin to thrombin, producing intravascular fibrin clotting and afibrinogenemia. The end result is local tissue necrosis and remote visceral hemorrhage and infarction.

Hyaluronidase, another component in the inoculum, acts as a local venom-spreading factor. (Enzymes which increase muscle excitability and neurotoxins found in Crotalus venom will not be discussed here.) The wide range of clinical manifestations of rattlesnake bite is probably owing to

variation in the relative concentrations of the toxins from one species to the next.

What is the renal lesion produced following rattlesnake bite? Renal lesions produced experimentally in animals by the administration of Crotalus venom vary from slight granular degeneration of the tubular epithelium to extensive exudative and hemorrhagic lesions of the glomerular tufts. The wide variation seen in animals suggests a correlation with the human response.

Amorim and Mello[1] described in detail the pathologic condition of the kidneys in three persons bitten by Crotalus terrificus terrificus. The significant findings were degeneration and desquamation of tubular cells of the ascending limbs of Henle, associated with intense interstitial inflammatory response predominantly in the intermediate zone of the kidney, characterized by neutrophilic leukocytes, edema and histiocyte proliferation. Hemoglobin casts were present in the distal convoluted tubules and collecting tubules. Glomeruli were spared. Proximal tubules showed cloudy swelling. Capillary and precapillary hyperemia was prominent. Grossly, multiple hemorrhagic foci in perirenal and renal tissues were noted. In short, the lesions produced are those of hemoglobinuric nephrosis. Whether these findings can be translated to North American Crotalidae is unknown. The lesion awaits description. Unfortunately renal biopsy was not done in the case reported herein.

Because of the minimal local tissue reaction about the site of the bite and the rapid onset of intense systemic response we believe that the patient received a direct intravenous inoculation of venom. The presence of a single fang mark indicates that the total volume of the inoculum was less than would ordinarily be expected. Having survived the initial impact, the patient's problem became one of severe although reversible renal failure.

If the renal lesion produced by North American Crotalus venom is intermediate tubular necrosis, it is most important that shock be prevented in order to avoid the superimposition of ischemic tubular necrosis upon the already damaged nephron. One wonders whether the judicious use of Mannitol® (a hexahydric alcohol) or other osmotic diuretic in the early phase of treatment might be indicated to support the circulation and maintain flow of urine.

Once renal failure is present, careful support and extracorporeal or intraperitoneal dialysis are indicated if this potentially reversible disease is to be overcome.

SUMMARY

The clinical syndrome of acute renal failure developed following inoculation of venom by a rattlesnake bite, apparently directly into a vein. Careful supportive care alleviated the seriousness of the initial impact and use of the artificial kidney provided the time for renal recovery.

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